CLINICAL CORRELATES OF EARLY BRAIN DAMAGE: RELATIONSHIP BETWEEN EEG AND PEDAL ASYMMETRY AS INDICES OF HEMISPHERIC LATERALITY AND PATHOLOGICAL LEFT-HANDEDNESS

BY

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A DISSERTATION PRESENTED TO THE GRADUATE COUNCIL OF THE UNIVERSITY OF FLORIDA IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA

1981

To Mom and Dad--for being there always

ACKNOWLEDGEMENTS

This project would have been impossible were it not for the support, guidance and coordinated effort of many individuals. My sincerest appreciation goes to my research assistants for their help during the year of data collection, and to Eileen Fennell and Carolyn Tucker for helping to make these undergraduate research students available to me. I would like to thank Hugh Davis, Eileen Fennell, Jim Willmore and Warren Rice for catching the few thermal tiles that slipped off, and keeping me from burning up upon re-entry. I would like to thank Janet Larsen, who not only provided continued support, but who inspired me to apply for the foundation fellowship which made this research year possible. I would also like to thank Randy Carter for his help with the statistical analyses, and Nancy Hurley who taught me the joys of the computer terminal. My gratitude also to Paul Satz, for his support and inspiration.

While I would like to thank the members of my committee collectively for their helpiful comments and continued support, I would like expressly to thank Warren Rice for taking over the helm and keeping me afloat, and Jim Willmore, who not only coordinated the efforts for data collection in the three centers used, but whose insatiable patience, medical expertise and ability to maintain his sense of humor throughout it all made this project possible. Finally, I would like to express my deepest

gratitude to Ken Heilman, whose ideas laid the groundwork for my master's research, which in turn provided the foundation for this doctoral project.

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CLINICAL CORRELATES OF EARLY BRAIN DAMAGE: RELATIONSHIP BETWEEN EEG AND PEDAL ASYMMETRY AS INDICES OF HEMISPHERIC LATERALITY AND PATHOLOGICAL LEFT-HANDEDNESS

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June 1981

Chairman: Warren J. Rice
Major Department: Clinical Psychology

The present study tests the hypotheses that alterations in body asymmetries (foot size differences) may reflect corresponding alterations in cortical dominance in individuals with a history of brain trauma, and that a relationship between pedal asymmetries, lesion location, age at lesion onset and manifest handedness may help differentiate normal from pathological left-handers.

Two hundred fifty adult epileptics and 50 medical controls (with normal EEGs) were studied. Individuals were classified as left- or right-handed based on their score on a handedness questionnaire. Experimental subjects were classified into early, middle and late seizure onset groups if their seizures began, or the event precipitating their seizures (when known) occurred before age 2, between the ages

of 2 and 17, or after age 17 respectively. EEG and CT scan reports were used to document lesion location. Information regarding age, sex, medical history and family history of left-handedness (familial sinistrality) was collected. Pedal asymmetry was assessed by tracing each bare foot onto a large data coding sheet. Pedal asymmetry was represented as right foot length minus left foot length.

Results indicate that the frequency of left-handedness in subjects with early onset left focal lesions was significantly greater than in control subjects or experimental subjects with middle or late onset seizures. The incidence of left focal lesions in left- and right-handers with early or middle onset seizures closely paralleled that predicted by the Satz model of pathological left-handedness (PLH). Individuals with late onset seizures did not show this predicted frequency.

The relationship between EEG focus and pedal asymmetry was significant only for subjects with early onset focal lesions. Subjects with early onset left focal lesions were found to have a significantly shorter right foot. The opposite was found for subjects with early onset right focal lesions. No sex or familial sinistrality differences were found across groups. CT scan results correlated highly with

EEG classification when CTs were read as abnormal, but this was not frequently the case.

Left-handers were classified into four groups as suspect for PLH, with early onset left focal lesion sinistrals considered highly suspect, middle onset left focal lesion sinistrals moderately suspect, late onset left focal lesion sinistrals low suspect, and control sinistrals or non-left focal lesion experimental sinistrals (regardless of onset) as not suspect. Pedal asymmetries were significantly different for the high suspect and non-suspect left-handers only, with the high suspects having a smaller right foot. Further analyses revealed that a right-left difference of .5 cm or more (right foot smaller) predicted PLH. The frequency of sinistrals with early onset left focal lesions falling beyond this classification cutoff point paralleled the incidence of PLH in sinistrals with left focal lesions predicted by Satz.

Four of the five sinsitrals with middle onset seizures reported that their hand preference changed from a dextral preference secondary to brain trauma, illness or surgery. However, only one individual, who had undergone a left frontal lobectomy, demonstrated a pedal asymmetry falling beyond the .5 cm cutoff. This suggests that beyond age 2, hand

preference can be altered without corresponding changes in pedal asymmetry, and that the presence of a significantly shorter right foot in a left hander may indicate the presence of an early onset left focal lesion and PLH. This is supported by the observation that all of the early onset left lesions were focal in nature.

Further documentation of the relationship between alterations in foot growth and corresponding alterations in cortical dominance (e.g. cortical speech representation) is needed to validate the diagnostic utility of pedal asymmetry measures as an index of PLH.

INTRODUCTION

Statement of the Problem

Review of the Pathological Left Handedness Literature

In the early 1900's a number of studies appeared in the literature (reviewed by Bingley, 1958) reporting a raised incidence of manifest left-handedness (14-22%) in retardate and epileptic populations, which represents approximately a two-fold increase over the base rate of left-handedness (7-13%) reported in normal populations (Coren & Porac, 1980; Dreifuss, 1968, Gordon, 1920; Mayet, 1902, cited in Gordon, 1920; Stier, 1911, cited in Bingley, 1958). Redlich (1908, cited in Bingley, 1958) studying epileptics, postulated that the association between epilepsy and left handedness was the function of a lesion to the left hemisphere, producing not only epilepsy, but a "slight, scarcely discernable right hemiparesis but sufficient to create a preference for the left hand in an otherwise natural right-hander" (Bingley, 1958, p.50). Similarly, Gordon (1920) hypothesized that the raised incidence of left-handedness observed in retardates was secondary to a left hemisphere lesion, causing both mental deficits and a slight hypofunction of the

right hand and hence switch in manifest hand preference to the contralateral, or left, hand. In 1945, Brain applied the term "pathological left-handedness" (PLH) to differentiate the innate sinistrals from those who become so secondary to early brain trauma or "pathology."

A corollary question was raised as to just how early a lesion must occur to cause such a switch in manifest hand preference. Penfield and Roberts (1959) noted that the frequency of left-handedness in their population of 522 adult epileptics who underwent unilateral temporal lobectomies for the control of intractible seizures dropped from 17% to 8.5% when all cases of cerebral injury prior to age 2 were excluded. This provides support for Satz's (1972, 1973) theory that the possibility of a transfer in manual preference is mostly likely if an injury to the dominant (left) hemisphere occurs during the period of greater plasticity of function (Lenneberg, 1967), before the later a..ization of cortical function becomes increasingly entrenched with the onset of language acquisition (approximately age 2). Moreover, physiological parameters of brain maturation (brain weight, axonal

myelination, glial cell proliferation) reach 60 90% of adult values by 18-24 months (Cheek, Holt & Mellits, 1972, Thompson, 1967, Wada, 1977) suggesting that by age 2, at least morphologically, much of the foundation for ultimate brain development has been clearly established.

An early onset lesion to the left hemisphere does not guarantee that a switch in manual preference will occur. Many individuals experiencing early left trauma will remain right handed and it is unlikely, despite Bakan's (1971, 1977) claim to the contrary, that all left-handers are pathological left-handers.

How then might one determine the frequency of pathological left handedness in a population of individuals with known left hemisphere damage?

In the early 1970's Satz (1972, 1973) proposed a mathematical model to predict the incidence of pathological left-handedness. According to the model, in a clinical (retardate or epileptic) population, the probability that a natural right-hander will switch to a left hand preference following an early unilateral left-hemisphere lesion (before age 2) is .21 The model further predicts that if an individual is left-handed,

the probability that the primary lesion is in the left hemisphere is .81, with a .44 probability of a left focal lesion in right-handers A third prediction posed by the Satz model states that if a left-handed clinical subject has a left focal lesion, the probability that he is a pathological left-hander is .71. Support for this hypothesis arose from the aforementioned work of Penfield and Roberts (1959). As previously stated, when those individuals with early onset left hemisphere lesions (n=49) were isolated, the incidence of left handedness in the remaining patients (n=18) dropped to 8.5%. This is consistent with the base rate of left handedness in the normal population. If one hypothesizes that these 49 left-handers with left-sided lesions of early onset were pathological left-handers, the frequency of these left handers amongst all left-handers with left brain trauma would be 49/67 = .73, which parallels the probability of occurrence proposed by Satz.

The Satz model also hypothesizes that the two fold increase in left-handedness observed in these clinical populations represents a 1:1 correspondence of natural to pathological left-handers, such that 50% of the

sinistrals in this population are pathological left handers. Lastly, this model predicts that the incidence of familial sinistrality amongst pathological left-handers should parallel that of normal right-handers, and should be less than that observed in normal left-handers where genetic factors would be involved (Annett, 1972, 1978; Boklage, 1978; Levy & Nagylaki, 1972; Rife, 1940).[1]

In recent years, the Wada techinque (Wada, 1949; Wada & Rasmussen, 1960) has been used successfully to identify the lateralization of cortical function, with specific focus placed on the cortical representation of speech, which is most commonly lateralized to the left hemisphere (Broca, 1861, cited in Branch, Milner & Rasmussen, 1964; Lenneberg, 1967).

This procedure involves intracarotid sodium amytal injections which cause a temporary inactivation of one hemisphere (Rasmussen & Milner, 1977). This technique has greatly assisted the identification of left-handers

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[1]In addition, cases of pathological right-handedness (PRH) also exists. However, the ratio of PLH to PRH is 11½ 1. This low frequency of PRH is restricted by the corresponding low base rate of natural left-handedness in the population (Satz, 1972).

with left-brain damage who demonstrate right hemisphere speech dominance, and thus would be presumed to be pathological left-handers.

It is quite likely that pathological left handedness also exists amongst individuals who do not fall into these clinical populations. Bakan (1971, 1977, 1978) and his colleagues (1973) report a 17% frequency of left handedness in a "normal" (college) population who were considered to be at high risk for birth trauma as a function of birth order. Although the relationship between left handedness and birth stress or birth order has been challenged (Annett & Ockwell, 1980; Hicks, Elliott, Garbesi & Martin, 1979, Hicks, Pellegrini, Evans & Moore, 1979, Schwartz, 1977), Coren and Porac (1980) have found a significant relationship between increased maternal age and a corresponding increased frequency of sinistrality, particularly in males. Bakan (1978) suggests that birth anoxia or hypoxia which has been reported to be the form of birth trauma most often producing central nervous system damage (Vick, 1976) and specifically motor disturbances of cerebral origin (Grinker, Bucy & Sahs, 1959) adversely

affects the pyramidal cells of the left motor cortex moreso than the right, although he provides no hypotheses as to why this is so. He suggests that the possible effects of such left hemisphere lesions (contralateral motor weakness, spasticity, paralysis) are transient, and recovery is rapid. He proposes that sinistrality might result from hypoxia-induced damage to the left motor cortex, but that detection of these functional defects becomes hampered by rapid cortical compensation and reorganization. It seems likely that there may exist individuals who experienced early brain trauma and subsequent alterations in lateral dominance, but who manifest little residual evidence of early pathology other than hand preference.

The identification of these pathological left-handers, in the absence of "hard" neurological evidence of cortical trauma such as seizure activity with abnormal electroencephalograph (EEG) recordings, abnormal computerized tomography (CT) scans of the brain, or results of invasive techniques such as the Wada procedure or the implantation of depth electrodes for EEG recordings has troubled investigators studying

the relationship between handedness and cortical lateralization of function. It is likely because of this inability to separate left-handers with undetectable brain damage from those without brain damage that the specialization of cortical function in sinistrals has continued to elude investigators. Satz, Baymur & Van der Vlugt (1979) stress that

> . . . These pathological left-handers (PLH), who are genotypically natural right handers, should be differentiated from natural left handers in any study addressed to the relationship between cerebral dominance and handedness. . . . Failure to separate out such pathological cases could obscure the results of this relationship. (p. 80)

PLH and Body Asymmetries

It becomes quite evident that a simple, non-invasive technique for the identification of PLH is essential if further developments are to be made in the understanding of lateralization of function in sinistrals.

The answer to this problem may lie in the exploration of body asymmetries that may correspond to the functional manual asymmetry.

Corballis and Morgan (1978) noted that

> Until very recently, most authors have treated handedness and cerebral lateralization in isolation from the many other systematic asymmetries which characterize both humans and lower animals. . . . As the biological nature of human laterality becomes more apparent, there seems no longer any fundamental reason why one should not seek common principles underlying handedness, cerebral lateralization, and the many other biological asymmetries to be found in nature. (p. 261)

Why might the study of asymmetries be important? The answer is quite simple. Normative data on average variance in body symmetry may provide much utility when profound deviations from this norm are observed. What might such aberrations in body symmetry mean? On a theoretical level, one wonders to what degree these manifest asymmetries reflect underlying asymmetries of the nervous system. Can a closer investigation of these left-right differences shed light onto the less readily measurable neural asymmetries?

The neurological literature suggests that morphological body asymmetries can result from early cortical insult. Trophic limb changes have been associated with severe early brain insult, as in infantile hemiplegia, which produces 'contralateral dysgenesis' (Critchley, 1971, p. 163). Vick (1976) states that ". . . early onset

of cerebral injury leads to a relatively prominent growth retardation of the affected limbs" (p 852). Grinker, Bucy and Sahs (1959) report that infantile hemiplegia or cerebral diplegia (Little's Disease) may cause gross malformations or developmental defects. Similarly, trophic changes, usually manifest in the bony skeleton, are also noted in patients with syringomyelia (Merrit, 1975).

Since body asymmetries have been observed in individuals with severe brain trauma, one wonders to what degree the development of body asymmetries can arise secondary to less severe cortical damage. Might not individuals with a less severe early onset focal lesion manifest similar yet correspondingly less severe trophic changes? Can an early lesion to the left hemisphere which may foster the manifestation of a left hand preference also foster an alteration in limb development? The present study is designed to address these questions, exploring the possibility that individuals with documented brain trauma, as measured by EEG, CT and a clinical history of epilepsy, may manifest concomittant asymmetries in limb development

and that a closer investigation of these limb asymmetries may prove useful in the identification of pathological left-handedness.

History of Asymmetry Research

Peripheral Body Asymmetry

One need hardly look farther than his own body to observe subtle bilateral asymmetries. Halperin (1931) traced the awareness of this characteristic feature of human physiology to the days of ancient Greece and Rome. He noted that sculptors of the day, with an apparent appreciation of these anatomical differences, fashioned the heads and bodies of their statues with distinct asymmetries.

These biological asymmetries came under scientific scrutiny throughout the nineteenth and early twentieth centuries, as anatomists, anthropologists and archeologists sought to quantify these structural differences in axial skeletal development. The first scientific investigation of body asymmetry was undertaken in 1822, when J.F. Meckel, a German anatomist, attempted to quantify the readily observable structural asymmetries.

Subsequent investigations throughout the following century focused primarily on the measurement of axial skeletal differences with respect to length and weight (Halperin, 1931, Ingalls, 1931, Latimer & Lowrance, 1965). While "it has been established that the two halves of the body in human species . . . are in reality never symmetrical" (Halperin, 1931, p 676), results of these studies proved inconsistent. Trends in the direction of body asymmetries were reported, but variability of the measures was large, and the observations were not supported statistically.

Contemporary investigators continue to debate the question of peripheral asymmetries, comparing bone and muscle mass differences (Abler, 1976, Chhibber & Singh, 1970, Jain & Jain, 1979, Pande & Singh, 1971) and continue to produce inconsistent results with large intersubject variability. Recently, Plato, Wood and Norris (1980) explored the relationship between peripheral bone asymmetries and functional laterality[2] as measured by hand preference. However, not only were their

[2]The difference between asymmetry and laterality must be clarified. While these terms have frequently been used interchangeably, within the context of this paper an important distinction will be made. Asymmetry

findings statistically non significant, but handedness was classified on the basis of grip strength Porac Prezlowski (1978) suggests that hand dominance may not be equivalent to hand preference This will become an important distinction that must be addressed when relationships between lateral preference (handedness and footedness) and lateral dominance (e.g. motor ability or strength) are hypothesized Although cytopasmic distribution and genetic codes have been hypothesized to account for the manifestation of body and organ asymmetries (see Corballis & Morgan, 1978, for review) these postulates have come under critical review This study will focus on the relationship between brain and body asymmetries Let us consider first the asymmetries inherent in the central nervous system.

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refers simply to the lack of equality It refers to the degree, or magnitude of difference (i.e. lack of zero difference), regardless of the direction of these differences. A laterality effect demands that a consistent direction of asymmetry be observed. No implications are made with respect to the magnitude of these left-right differences.

Cortical Structural Asymmetry

The history of the study of cerebral dominance begins with the phenomenon of aphasia. Broca (1861, cited in Branch, Milner & Rasmussen, 1964) and Wernicke (1874, cited in Rubens, 1977) observed that lesions in specific regions of the left hemisphere, almost entirely within a ring of cerebral cortex that forms the upper and lower borders of the Sylvian fissure, interfere with language function.

The literature abounds with ample documentation of left hemisphere dominance subserving language function in most individuals. There is disagreement, however, as to whether this functional asymmetry is reflected in corresponding cortical asymmetry While LeMay (1976) reports numerous morphological cerebral asymmetries, Whitaker and Selnes (1976) cite several studies which note large individual differences in cortical topography. Even more perplexing, however, are the findings of Wada, Clarke and Hamm (1975) who suggest that the left frontal operculum, which includes Broca's area, is in fact smaller in surface area than its right counterpart. They added that it is likely that the total cortical surface area of this region might

in fact be greater on the left due to the possibility of greater fissuration.

A multitude of studies provide support for a functional-anatomical relationship. Cunningham (1892, cited in Rubens, 1977) and Eberstaller (1890, cited in Rubens, 1977) found the left Sylvian fissure to be longer in a significant number of cases. Rubens (1977) cited a number of early studies which demonstrate

> ...that this asymmetry occurs posterior to the central sulcus and is accompanied by asymmetries of the parietal and posterior temporal operculi, including the region of the planum temporale [an extension of Wernicke's area] which were longer on the left side. (p. 503)

Geschwind and Levitsky (1968) and Rubens (1977) supported these findings, documenting that the planum temporale is significantly longer on the left side in 65% and 69% respectively of normal adult brains. This difference has also been strongly associated with differences in the height of the Sylivian point. LeMay (1976) suggested that the Sylvian point is higher on the right because of increased fissuration on the left between the central sulcus and posterior end of the Sylvian fissure, reflecting a greater

quantity of cortical surface area. Rubens (1977) noted that the divergence between the left and right Sylvian fissure occurs posterior to Heschl's gyrus.

Despite these reported asymmetries favoring enhanced left hemisphere development, Walker (1980) reports that the right hemisphere has been found to weigh more than the left (LeMay, 1976), and in general, the front of the human brain is wider on the right, while the posterior regions are wider on the left Steklis (1978) reports that anterior subcortical, largely limbic, structures are also found to be larger on the right. He speculates that this may reflect the right hemisphere dominance for processing of emotional content, but adds that the relationship is, at best, correlational.

Perhaps even more fascinating is the observation that cortical asymmetries may manifest prenatally. Chi, Dooling and Gilles (1977) suggest that the right hemisphere leads the left in prenatal growth, and in general, matures sooner than the left hemisphere (Taylor, 1969). This would be consistent with the reported predominance of left handedness during the first nine months (Seth, 1973). Whitaker (1978) notes that an early right hemisphere maturation is clearly adaptive, with such right hemisphere dominant functions as

facial recognition or the processing of environmental sounds being essential during an infant's preverbal lifetime.

Moreover, the corresponding morphological symmetries have been noted in fetal as well as adult brains, suggesting that lateralization of function may begin prenatally. Cunningham (1892, cited in Rubens, 1977) observed asymmetries in Sylvian fissure length in fetuses ranging from 7½ to 8½ months. Rubens (1977) cites a number of studies which report morphological asymmetries as early as the 29th gestational week. LeMay (1976) notes that as early as the 16th gestational week, the right Sylvian point was higher in all 10 brains studied which, she adds, "suggests that thetemplate for cerebral dominance is present before birth" (p. 357). Moreover, the direction of tonic neck reflex at birth and hand preference at age 10 has been shown to be significantly correlated (Gesell & Ames, 1947), further supporting the findings of early lateralization of function.

Structural/Functional Asymmetry and Environmental Influences

The relationship between morphological asymmetries and manifest functional specialization has been the subject of intense investigation since the work of Broca (1861, cited in Branch, Milner & Rasmussen, 1964) and Wernicke (1874,

cited in Rubens, 197;). While these early investigators were limited to the exploration of brain behavior relationships in brain-injured populations, the introduction of dichotic listening and tachistoscopic technique has permitted psychologists to study cerebral lateralization of function in normal subjects as well (see Hécaen & Albert, 1978, for review).

One of the most extensive areas of research within the field of brain behavior relationships is that between cerebral lateralization of function and manifest hand preference. Whether hand preference is culturally (Blau, 1945, cited in Corballis & Beale, 1976), genetically (Annett, 1972, 1978, Levy & Nagylaki, 1972), biologically (Corballis & Beale, 1976, Corballis & Morgan, 1978), environmentally (Collins, 1977, Siegel, 1978) or pathogenically (Bakan, 1971; Bakan, Dibb & Reed, 1973) determined has been the subject of much debate. Brain (1945) suggests that handedness is not absolute, but rather a question of degree Bingley (1958) feels, however, that this is true only for sinistrals. Coren and Porac's theory (Coren & Porac, 1980, Porac & Coren, 1978) that the behavioral expressions of lateral preference are most likely multiply determined seems most logical.

The relationship between prenatal morphological asymmetries and subsequent functional specialization noted above provides some support for a biological rather than cultural/environmental model for the development of manual hand preference (Levy, 1974, 1977; Corballis & Morgan, 1978). Moreover, Witelson and Pallie (1973) suggest that the asymmetries observed in the neonate do not support the argument that hand preference in turn determines cerebral dominance, since these anatomical asymmetries can be observed before any learning effects, specifically language acquisition and unimanual hand preference, can manifest. They further suggest that

> The observed neonatal anatomical asymmetry provides a structural basis for the adult pattern of lateralization of language functions and it is such biological structures, rather than the experiential factors, which are the determining factors predisposing the left hemisphere to become the major hemisphere in mediating language functions. (p. 644)

Environmental factors such as birth trauma, childhood illness or injury and other central nervous system pathogens can disrupt this underlying pattern of cortical lateralization, favoring left hemisphere dominance for speech and manual skills, and right hemisphere dominance for

visuospatial skills. Studies by Milner (1975) and her associates (Branch, Milner & Rasmussen, 1964, Rasmussen & Milner, 1977) in their work with early onset epileptics and Dennis and her colleagues (Dennis & Whitaker, 1977, Kohn & Dennis, 1974 a,b) with hemidecordicates have demonstrated that

> If one hemisphere is impaired, whether by developmental anomaly, birth trauma, or some disease process occurring shortly after birth, other parts of the brain do, to some extent, acquire the functions which would otherwise be performed by the parts that have failed to develop . . . (or have been) destroyed. (Smith, 1974, p. 10)

Milner's work suggests that injury to the speech areas of the left hemisphere from birth through age 6 can produce an alteration in cerebral dominance, with an increase in right hemisphere or bilateral speech representation (as determined with the Wada technique) and on increase in left handedness.

In the 1977 study (Rasmussen & Milner, 1977), Milner presents diagrammatic representations of lesion locations, and provides compelling evidence that the lesion must encroach upon speech areas to produce an alteration in cortical speech representation. However, the relationship between language lateralization

and manifest handedness is unclear. While she reports an overall increase in manifest left-handedness and states that "an early lesion that does not modify hand preference is on the whole unlikely to change the side of speech representation" (1977, p. 359), it is unfortunate that she reports hand preference for only two of the 17 cases illustrated.

Thus, the relationship between early left hemisphere trauma, cortical dominance and handedness unfortunately remains unclear.

The investigation and comprehension of cortical specialization in left handers as a whole is further limited by the inability to separate those ". . . left-handers with undetectable brain damage from those without brain damage" (Levy, 1974, p. 170). However, in her most recent investigation (Levy & Levy, 1978) Levy may have developed just such a method.

Until the Levy and Levy (1978) study, few investigators have addressed the relationship between body asymmetries and corresponding asymmetries in cortical development. Levy and Levy addressed this question using pedal asymmetries (differences in foot size).

The selection of the foot in the assessment of asymmetry is appropriate for a variety of reasons. Changes in pedal development have been reported in individuals with documented brain insult. Grinker, Bucy and Sahs (1959) report that developmental defects secondary to cerebral mono and diplegia is most severe in, and sometimes limited to, the legs (p. 515) Moreover, Heilman[3] points out that methodologically, the measurement of the foot is preferential because of increased accuracy. Measurement of the hand is hampered by the difficulty in assessing precisely the point at which the hand ends and the wrist begins. Morgan (1977) postulates that handedness could account for axial skeletal differences in the upper extremities, and that possible growth differences might occur secondary to use. If this were so, the measurement of these asymmetries might reflect nothing more than artifact. In the foot, however, where differences would less likely be influenced by handedness, similar interactions would not be expected. If large pedal asymmetries were noted, it may more likely reflect possible underlying pathology.

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[3]Personal communication, 1978.

Moreover, foot preference does not necessarily correspond to hand preference (McBurney & Dunn, 1976, Porac & Coren, 1978) and the former may in fact have been assessed inaccurately in studies utilizing kicking as an index of foot preference. Friedes (1978) suggests that in a test for foot dominance, children would inevitably kick with the weaker leg, and the relatively impaired side would be assigned dominant status, when in fact the dominant leg was being used to maintain the body's upright stature. Thus, he adds, "it appears that 'dominance' may reflect an obligatory compensation for unrecognized pathology" (p. 134). Similarly, Vanden-Abeele (1980) notes that the assessment of lower limb dominance is compounded by a variety of postural (balancing on one leg) locomotor (running stride length) and operant (playing hopscotch) tasks issued to determine limb dominance and differing bilateralizations of the lower limbs can be found. Moreover, he notes that hopping is controlled by hip and knee joints, and should not be considered a foot activity. In sum, Vanden-Abeele calls for a distiction between leggedness and footedness in the determination of limb dominance or limb preference. Measurement of foot length, however, requires no assumption of limb preference or

dominance, and has been found to be a reliable measure given that an individual is standing with equal weight placed on both feet (Butlin and Foulds, 1963, cited in Stone & Jones, 1968). Using pedal measurements, Levy and Levy (1978) found that sex as well as handedness is strongly related to pedal asymmetry, with right-handed males having larger right feet, while right-handed females have larger left feet. The reverse was reported for left-handed individuals. This novel finding, if true, would compound the neurological data regarding the relationship between unilateral limb development and severe cortical insult.

There were, however, several methodological problems in the Levy and Levy study regarding their rating scale, statistical analysis, sample composition and measurement procedures which led this investigator to question the validity of their findings. A replication study was performed to correct for these errors (Yanowitz, Satz & Heilman, 1981). The replication study failed to support any of the Levy and Levy findings. No differences were found in the direction of pedal asymmetries for males or females, dextrals or sinistrals, with or without a family history of sinistrality for either foot length or width. Similarly, the findings of

Pomerantz and Harris (1980) failed to support the Levy and Levy findings.

Some additional findings surfaced in the Yanowitz, Satz and Heilman (1981) study which warrant further investigation. While no mean differences were observed between the pedal asymmetry for dextrals or sinistrals, the variability of the pedal asymmetry was greater for left-handed males than for females or right-handed males. This appeared to be a function of three individuals who showed a robust difference (> 2 S.D) in the size of their two feet. It is possible that these pedal asymmetries could occur by chance factors alone. However, these three individuals deviated so markedly from the group means, it appears that something other than normal variance may account for these pedal asymmetries.

A closer investigation of these three outliers revealed that the two individuals with the greatest pedal asymmetry (1.8 cm and 1.3 cm) had a significantly shorter right foot. This would be consistent with the trophic changes associated with early brain trauma found in clinical populations (Grinker, Bucy & Sahs, 1959, Merritt 1975; Vick, 1976). The presence of a markedly shorter right foot in left-handers, and specifically in males, who are known to be

at greater risk for birth injury and disease (Taylor & Ounsted, 1972), indirectly suggests the presence of path ological left-handedness in these individuals. However, this study employed a normal high school and college population. A better understanding of the relationship between pedal asymmetry, handedness and cerebral dominance may arise from an investigation thereof in a clinical population with cortical trauma.

Recently, Satz and his colleagues (Satz, Baymur & Van der Vlugt, 1979, Silva and Sat., 1979) found that the raised incidence of manifest left handedness in epileptic and retardate populations was strongly related to the presence of unilateral left hemisphere lesion as represented by EEG abnormalities.

The Satz, Baymur and Van der Vlugt (1979) article presents the differential frequency of left focal lesions noted in four studies of epileptic and retardate dextrals (41-68%) and sinistrals (75-92%) as support for the Satz (1972, 1973) model of PLH. However, three of the four studies fail to report the age of onset of the lesion, which is an integral part of the Satz model. The findings overall are, however, consistent with Milner's observation of an increased frequency of left handedness in epileptics with early onset left temporal lobe lesions.

If early left focal lesions do produce an increase in manifest left-handedness and an alteration in cortical speech representation as the Satz and Milner studies suggest, might they also produce an alteration in limb development? If a relationship between handedness (left), lesion location (left), onset age (before age 2) and pedal asymmetry (shorter right foot) exists, this would provide support for the development and use of pedal asymmetry measures as a simple non-invasive clinical tool in the determination of cerebral dominance, isolation of early brain insult and documentation of pathological left-handedness.

Purpose

The present study addresses the following questions:

1) Is there a relationship between handedness, pedal asymmetry, and EEG abnormalities?
2) Is age of onset of the lesion related to handedness, pedal asymmetry and EEG abnormality?
3) If so, can the exploration of pedal asymmetry be useful in differentiating those sinstrals who are at high risk for pathological left-handedness, in accordance with the Satz (1972, 1973) model, from those sinistrals who are not at risk for PLH?

4) Is pedal asymmetry related to sex or family history of sinistrality?

Several hypotheses can be drawn from these questions. Based on Satz's model of PLH and neurological evidence of patterns in hemi-syndromes, one might predict that a relationship exists between early brain trauma and decreased development of the contralateral limb. Moreover, age of onset (early) and location of lesion (unilateral) should affect the degree to which the pedal asymmetry, when it occurs, correlates with manifest hand preference. One would hypothesize that an early lesion to the left hemisphere would increase the likelihood of manifest sinistrality, and correspondingly the development of a shorter right foot. However, if damage occurs after lateral dominance has produced a hand preference, could it affect the pedal develop ment without altering manifest hand preference? Conversely, with a much larger area of cortex involved in motoric and somasthetic control of the hand relative to the foot (Gardner, 1968; Penfield & Jasper, 1954) it is indeed possible that a lesion causing hypofunction of the hand may not be large or severe enough to produce an underdevelopment of the lower limbs as well. However, since we are as yet uncertain what areas of the brain control limb growth and

development, it is unwise to generate hypotheses as to the precise nature of the relationship between pedal asymmetry and manifest hand preference. Would robust pedal asymmetries (smaller right foot) occur without a change in manifest hand preference, or might pedal asymmetry be a more sensitive measure, occurring only in conjuction with unilateral left lesions and a switch in hand preference? If the latter were so, pedal asymmetry measures could prove to be a sensitive measure, not of left handedness per se, but of PLH, which corresponds to the presence of an abnormal left sided EEG, left handedness, and a low incidence of family history of sinistrality. In addition, one would expect a higher frequency of males amongst the group of sinistrals expected to be at risk for PLH, because of their greater susceptibility to early trauma Lastly, if these pathological left handers are natural dextrals, the frequency of familial sinistrality should parallel that seen in the right-handed population.

METHOD

Subjects

Two hundred forty-two adult volunteers (ages 17-55) with a history of epilepsy were recruited from Shands Teaching Hospital (STH), the Gainesville VA Medical Center (GVAMC), and the Epilepsy Association of Central Florida, Orlando, during the period of August, 1979 - September, 1980. Subjects from STH and GVAMC consisted of neurology patients who presented at the neurology or seizure out-patient clinics, or who were inpatients on one of the neurology wards. Subjects from the Epilepsy Association of Central Florida were similarly recruited during a routine visit to the clinic therein.

Fifty-six subjects (ages 17-55) with no history of clinical seizures and with normal electroencephalograph (EEG) recordings were recruited to serve as control subjects. These individuals were recruited from the aforementioned neurology clinics at STH and GVAMC and from a number of non-neurology services (medical and psychiatric) referring patients to the EEG laboratories of these two facilities. Patients were typically referred because of a reported history of dizziness, headaches, illness or trauma and for which epilepsy need be ruled out as a differential

diagnosis. Data on all subjects were screened by Dr. L. J. Willmore, Department of Neurology, GVAMC, Associate Professor, Departments of Neurology and Neuroscience, University of Florida. Any subject whose inclusion into either the experimental or control group was not clearly discernable was eliminated from this investigation.

Subjects with incomplete data were also eliminated, as were those with a history of polio or arteriosclerotic disease to minimize the possibility that EEG abnormalities or body asymmetrics could be accounted for by factors other than those under investigation.

Following the screening procedure, 230 epileptic adults and 50 non-epileptic adult controls remain for investigation.

Materials and Procedure

All subjects were asked to sign a consent form indicating their volunteer participation in this study (Appendix A). The hand used to sign this consent form was noted by the investigator. Subjects were also asked to state their hand preference, and completed a 12-item hand preference questionnaire (Briggs & Nebes, 1975, Raczkowski, Kalat & Nebes, 1974). Information regarding age, sex, family history of sinistrality (that of parents and siblings) was collected. A subject was considered to have a positive history of familial sinistrality (FS+) if one or more of

his or her parents or siblings were classified as left-handed or ambidexterous. Medical history, including the etiology and onset age of epilepsy when appropriate was collected from the patient, medical files, and family members when available. EEG reports and computerized tomography (CT) scan reports when available were also collected from the medical records.

Under the supervision of Dr. L. J. Willmore, the EEGs were classified as normal or abnormal. EEGs were considered abnormal if epileptiform activity was noted. Within the abnormal classification EEG results were further classified according to lesion location[4] (Appendix B). Computerized tomography (CT) scan results were also classified according to site and type of abnormality (Appendix C).

Foot measurements were obtained by tracing each bare foot outline onto a large data coding sheet. All measurements were performed on a smooth tile floor. Subjects were instructed to place equal weight on both feet. Foot length was calculated in centimeters (cm). Measurement was obtained by drawing perpendicular lines from the most

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[4]Individuals with a long history of epilepsy often develop a seizure focus, known as a "mirror focus," contralateral to the original lesion site. When these mirror foci are noted, the site of the original lesion is used for classification.

extreme points of measurement (Appendix D) in accordance with a procedure which was found to be a reliable and valid measure of foot length (Yanowitz, Satz & Heilman, 1981). Pedal asymmetry was computed as right foot length minus left foot length.

Statistical Analyses

Age Comparison

Mean age differences between the control and experimental subjects were compared with the analysis of variance (ANOVA) procedure of the Statistical Analysis System (SAS) (Helwig & Council, 1979).

Handedness

Hand preference was scored on a five-point scale (always left, usually left, no preference, usually right, always right) by asking the subject to indicate which hand would normally be used to perform each of 12 activities. Total scores range from 12 to 60. The correlation between the total score on the hand preference questionnaire and (1) stated hand preference (left, right or ambidexterous) and (2) preferred writing hand (left or right) was assessed utilizing the point biserial correlation procedure. A criterion for handedness (left or right) was then determined by defining the cutoff point on the hand preference questionnaire which maximized the correct classification of stated

hand preference.[5] The test for significance of a proportion (Bruning & Kintz, 1968) was used to compare the proporation of left handers with early onset lesions to the base rate of left handedness in the population.

Onset Age (Group Classification)

Age of onset was defined as the age of onset of the incident (trauma, illness, etc.) which precipitated the seizure. When the etiology of the seizure was unknown, the seizure onset age was utilized as the onset age. Subjects were then classified into four groups.

Group 0 (no onset) - control subjects

Group 1 (early onset) - experimental subjects with onset age from birth through age 2.

Group 2 (middle onset) - experimental subjects with onset age between ages 2 and 17.

Group 3 (late onset) - experimental subjects with onset age greater than 17.

EEG Classification

Classification of abnormal EEGs was collapsed into six categories:

(1) Right anterior quadrant
(2) Right posterior quadrant
(3) Left anterior quadrant
(4) Left posterior quadrant
(5) Diffuse/generalized
(6) Bilateral

[5]For the three individuals whose hand preference was reported as ambidexterous, the criterion point that was determined caused their correct classification with respect to their preferred writing hand.

CT Scan Classification

Due to the paucity of abnormal CT Scan reports in this sample, classification was collapsed into three categories

(1) Right hemisphere involvement
(2) Left hemisphere involvement
(3) Diffuse involvement

Pedal Asymmetry (Foot Difference) Comparisons

The ANOVA statistic for unbalanced groups utilizing the general linear model (GLM) procedure of the SAS package was used to address the relationship between pedal asymmetry and (1) handedness, (2) EEG focus, (3) CT scan focus, (4) onset (group), (5) sex, and (6) familial sinistrality across all subjects. Post hoc analyses of mean differences were explored with Duncan's multiple range test and t test comparisons.

Comparisons of Subjects with Focal Lesions

The relationships between handedness, EEG focus, CT scan focus, onset (group), sex and familial sinistrality were explored in individuals with focal lesions utilizing the χ^2 statistic. T tests compared mean asymmetry differences as a function of EEG focus across all experimental subjects and by each onset age group. This subsample of individuals with focal lesions was selected for the purpose of consistency with previous studies exploring cortical/functional asymmetries.

PLH Suspect Classification

To address question 3, all left-handers were first classified into four groups (high suspect for PLH, moderate suspect, low suspect and not suspect) in accordance with the model of PLH proposed by Satz (1972, 1973). A sinistral was classified as a high suspect for PLH if he or she had a left focal lesion and early onset. A moderate suspect is a sinistral with a left focal lesion and onset between ages 2 17, while a low suspect is a sinistral with a left focal lesion occurring after age 17. An individual is not suspect if he or she is a sinistral has a non-left focal lesion (regardless of onset) or with no lesion history (control subject).

The GLM statistical procedure was utilized to explore overall pedal asymmetry differences across these four "suspect" groups, and Duncan's multiple range test explored post hoc mean differences. The Spearman correlation coefficient was used to explore the degree of correlation between the foot difference and suspect group. High and moderate suspects were then classified as PLH+ and low and non-suspects as PLH . ANOVA was used to compare mean asymmetry differences and yielded an index (r^2) of the degree of variability in pedal asymmetry accounted for by the dichotomized PLH classification.

PLH Prediction

Based on the results of the previous analyses, question 3 was addressed. A classification function formula, based on the linear discriminant analysis described by Anderson (1958, p. 131) but simplified because of the use of only one variable (foot difference) was calculated. This formula was then used to determine the foot difference (pedal asymmetry) cutoff point which minimizes the misclassification of a subject as either highly suspect or not suspect for PLH.[6] A subject will be classified as highly suspect for PLH if

$$FD \leq \frac{-\sigma^2 \times \log_e \left(\frac{P/NS}{P/S} \right)}{\mu_{NS} - \mu_S} + \frac{\mu_{NS} + \mu_S}{2}$$

Where

FD	=	foot difference
$\log_e$	=	natural log
P/NS	=	probability of not suspect for PLH
P/S	=	probability of high suspect for PLH
σ^2	=	assumed common variance
μ_S	=	population mean of high suspect for PLH
μ_{NS}	=	population mean of not suspect for PLH

[6] This formula was calculated by Randy Carter, Assistant Professor of Biostatistics, University of Florida.

RESULTS

Analysis of variance yielded no age difference between control (mean age = 33.5) and experimental (mean age = 32.5) subjects.

As Table 1 illustrates, the questionnaire scores and both self-report of handedness (right, left, ambidexterous) and writing hand (left, right) were highly correlated, with 79% and 80% of the variability in questionnaire scores accounted for by differences in self-reported handedness and writing hand respectively.

Handedness classification was determined by defining the questionnaire cutoff point which maximized the correct classification of stated hand preference. The latter was selected because of its independence from the 12 item questionnaire.[7]

Table 2 demonstrates that a cutoff point between 36 and 37 resulted in only one self-classified dextral and two self-classified sinistrals being differentially categorized. The cutoff point further resulted in the three

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[7]The slightly higher correlation between total handedness score and writing hand may be secondary to the fact that writing hand is one of the 12 items in the questionnaire, and may then spuriously involate the correlation between the individual variable and overall score.

Table 1

Point Biserial Correlation (r_{pb}) and Variance (r^2) of Handedness Measures Across All Subjects

	Questionnaire Score	Self-report
Questionnaire Score	1.00	r_{pb} 0.89 *
Self-report		r^2 0.79 *

	Questionnaire Score	Writing hand
Questionnaire Score	1.00	r_{pb} 0.89 *
Writing hand		r^2 0.80 *

* $p < .0001$

Table 2

Classification of Handedness

Stated Hand Preference[a]	Subject	Questionnaire Score				Total
		≤ 36 (Left)		≥ 37 (Right)		
Right	Control	0	(1)	43	(245)	246
	Experimental	1		202		
Left	Control	5	(32)	1	(2)	34
	Experimental	27		1		
Total			33		247	280

[a]Ambidexters are classified according to preferred writing hand

self-classified ambidexters being correctly classified according to their writing preference. While there was no overall difference in the distribution of handedness scores for the control or experimental subjects (Table 2), the experimental sinistrals scored as significantly more left-handed (mean score = 17.8) than did the control left handers (mean score = 26.3) when this classification scheme was used, $F\ (1,31) = 6.29$, $p < .02$. No differences were found for the handedness scores of the experimental and control dextrals (mean score = 55.5 and 55.2 respectively).

The overall frequency of left handedness was not significantly different for control (12%) and experimental (11.74%) subjects when all seizure types were combined. Similarly, no overall relationship between sex and handedness was found (Table 3). Although more males were left-handed in both the control (13.8%) and experimental (13.5%) groups relative to females (9.5% and 9.9% for the control and experimental groups respectively), these differences were non significant. The paucity of left handed subjects precluded a within group (seizure onset group) sex by handedness analysis, but observation of the data suggests that no sex differences would be found. However, a significant sex effect was found across seizure onset groups, $\chi^2\ (3) = 17.95$, $p < .0004$, with a greater than expected number of males observed in the late onset seizure group. It appears

Table 3

Frequency of Handedness and Sex by Group

Hand[a]	Sex[b]	Groups 0 Controls	1 Early Onset	2 Middle Onset	3 Late Onset	Total
Right		44 (25M) (19F)	47 (19M) (28F)	76 (35M) (41F)	80 (56M) (24F)	247 (135M) (112F)
%		88%	88.4%	86.4%	91.9%	88.2%
Left		6 (4M) (2F)	8 (4M) (4F)	12 (6M) (6F)	7 (7M) (0F)	33 (21M) (12F)
%		12%	14 [illegible]	[illegible]	8 [illegible]	11.8%
	Male	29	41	41	63	156
	Female	21	32	47	24	124
Total		50	65	88	87	280

[a]Handedness by Group χ^2 NS

[b]Sex by Group χ^2 (3) = 17.95, $\underline{p}$ < .0004

that this finding is invalid, secondary to the inclusion of the 49 subjects from the Veterans Administration (VA) Medical Center (48M, 1F), all of whom had late onset seizures, and hence were classified as members of Group 3. The inclusion of these individuals would artificially distort the overall frequency of sex across groups by increasing the frequency of males in Group 3. Indeed, when these subjects are omitted, the observed sex effect disappears (Table 4). Moreover, despite the loss of all left handers from Group 3 with the deletion of VA subjects, the handedness effect remains non significant.

Within the experimental subjects, no differences were found in the overall frequency of left-handedness for individuals with focal (12.8%) or diffuse (9.9%) lesions. However, when the subjects were classified by age of onset, a strong association was found within the early onset seizure group. All 100% of the sinistrals in this group were found to have focal lesions, and of those individuals with focal lesions, 22.2% were left-handed. The relationship between handedness and lesion (focal versus diffuse) was significant, χ^2 (1) = 4.94, p < .02. In the middle and late onset seizure groups, no relationship between handedness and lesion focus was found. A test of binomial proportion revealed that the frequency of left-handedness amongst

Table 4

Frequency of Handedness by Group
VA Subjects Deleted

Hand	Sex	Group 0	1	2	3	Total
	M	25	19	35	15	
Right						
	F	19	28	41	23	
	n	44	47	76	38	205
	(%)	(88%)	(85.4%)	(86.4%)	(100%)	(88.7%)
	M	4	4	6	0	
Left						
	F	2	4	6	0	
	n	6	8	12	0	26
	(%)	(12%)	(14.6%)	(13.6%)	(0%)	(11.3%)
Total		50	55	88	38	231

χ^2 NS for sex and handedness

sinistrals with early onset left focal lesions (22.2%) is significantly higher than the base rate within the population (approximately 10%), $z = 2.4$, $p < .008$.

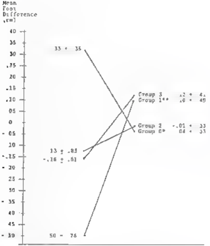
Analysis of variance of pedal asymmetry (right foot length minus left foot length) across all subjects ($n = 280$) revealed no main effect for seizure onset group, sex, EEG, CT abnormality or familial sinistrality. That is, no mean asymmetry difference was found between the different classifications (levels) of these variables. A main handedness effect was found, $F\ (1,268) = 5.05$, $p < .02$. Right handers had slightly larger right feet (mean asymmetry = 0.05 cm) while left handers had slightly larger left feet (mean asymmetry = 0.14 cm). While they are significantly different from each other, these differences are not different from zero. A significant interaction between handedness and onset group was found, $F\ (3, 268) = 5.02$, $p < .0004$, as illustrated in Figure 1, with mean pedal asymmetries differing for the dextral and sinistral control (Group 0) and early onset (Group 1) subjects. T tests revealed that left-handed control subjects had smaller left feet, while control right-handed subjects had smaller right feet, $t\ (48) = 2.53$, $p < .0004$. The reverse was seen for early onset seizure subjects, $t\ (53) = 2.97$, $p < .01$.

Table 5 presents the distribution of EEG abnormalities by handedness across all experimental subjects, revealing

Table 5

Frequency of EEG by Handedness for All Experimental Subjects

		EEG Focus							
Hand	Frequency	Normal	Right Anterior	Right Posterior	Left Anterior	Left Posterior	Generalized (Diffuse)	Bilateral	Total
Right	n	15	58	4	66	2	46	12	203
	Row %	(7.4%)	(28.6%)	(2.0%)	(32.5%)	(1.0%)	(22.7%)	(5.9%)	(88.3%)
	Column %	(90.8%)	(93.5%)	(80.0%)	(83.5%)	(66.7%)	(88.5%)	(85.7%)	
Left	n	0	4	1	13	1	6	2	27
	Row %	(0.0%)	(14.8%)	(3.7%)	(48.1%)	(3.7%)	(22.2%)	(7.4%)	
	Column %	(9.2%)	(6.2%)	(20.0%)	(16.5%)	(33.3%)	(11.5%)	(6.2%)	(11.7%)
Total		15	62	5	79	3	52	14	230
%		(6.5%)	(27.0%)	(2.2%)	(34.3%)	(1.3%)	(22.6%)	(6.1%)	



*Group 0 t (46) = 2 53, p < 01
**Group 1 t (53) = 2 97, p < 004

Figure 1. Group by Handedness Interaction on Pedal Asymmetry

that only 3.5% of the subjects presented with focal posterior lesions. Focal EEG classification was reduced to two categories (right and left hemisphere) because of the paucity of subjects with posterior lesions.

In the subset of individuals with focal lesions (right or left) ($\underline{n}$ = 149) no significant differences were found in the distribution of either sex or familial sinistrality as a function of EEG focus across all subjects or by onset group. Similarly a χ^2 comparison of familial sinistrality by handedness in individuals with focal lesions yielded no significant differences.

Of these 149 individuals, only 87 had undergone CT scans. Of those, 63 were found to be normal. Table 6 presents the relationship between focal EEG and CT scan findings. When a CT scan is read as abnormal, it correlates highly with EEG findings (r = .92). However, CT scans were found to be abnormal in only 27.5% of the cases of individuals with known cortical lesions as reflected by EEG abnormalities and clinical history of seizures.

Table 7 presents the relationship between EEG focus and manifest hand preference across all experimental subjects and by onset group. This relationship is significant only for subjects with seizure onset before adulthood, Group 1 χ^2 (1) = 5.79, $p < .02$, Group 2 χ^2 (1) = 3.60, $p < .05$, Groups 1 and 2 combined χ^2 (1) = 9.57, $p < .005$. The

Table 6

Frequency of CT Scan by EEG Focus
(Focal Lesions Only)

	CT Scan Focus			
EEG Focus	(Normal)[a]	Right	Left	Total Abnormal
Right	(28)	9	1	10
Left	(35)	0	14	14
Total Abnormal	(63)	9	15	24

χ^2 (1) = 20.16, $p < .0001$[b]

r = .92

$\underline{r}^2$ = 84.10

[a]Not included in χ^2 computation.

[b]This statistic may not be valid because of the sparcity of the table.

Table 7

Handedness by Group as a Function of Lesion Focus
(Focal Lesions Only)

		EEG Focus			
Group	Hand	Right n (%)	Left n %	Total n %	Significance[a]
1	R	17 (60.7)	11 (39.3)	28 (77.8)	5.79**
	L	1 (12.5)	7 (87.5)	8 (22.2)	
				36	
2	R	26 (57.8)	19 (42.2)	45 (88.2)	3.60*
	L	1 (16.7)	5 (83.3)	6 (11.8)	
				51	
3	R	19 (33.3)	38 (66.7)	57 (91.9)	2.60
	L	3 (60.0)	2 (40.0)	5 (8.1)	NS
				62	
All	R	62 (47.7)	68 (52.3)	130 (87.2)	3.06
	L	5 (26.3)	14 (73.7)	19 (12.8)	NS
				149	
1&2	R	43 (58.9)	30 (41.1)	73 (83.9)	9.37***
	L	2 (14.3)	12 (85.7)	14 (16.1)	
				87	

[a] χ^2 (1) for all groups

* $p < .05$

** $p < .02$

*** $p < .003$

frequency of left focal lesions in sinistrals with early or middle onset seizures (Groups 1 and 2) was 87.5% and 83.3% respectively, with an average frequency of 85.7% across the two groups. This contrasts with the 40% frequency of left focal lesions in sinistrals with late onset seizures. Similarly, the incidence of left focal lesions in dextrals was only 39.3% and 42.2% in Groups 1 and 2 (41.1% combined) compared with an incidence of 66.7% in dextrals with late onset seizures. Moreover, it is observed that the frequency of left handedness is 22.2% in individuals with early onset seizures, which is consistent with that reported for retardate and early focal lesion subjects (Penfield & Roberts, 1959; Rasmussen & Milner, 1977; Silva & Satz, 1979). The incidence of left handedness in the middle and late onset groups (11.8% and 8.1% respectively) parallels that reported in normal populations.

Similarly, the relationship between EEG focus and pedal asymmetry is significant only for subjects with early onset seizures, $t\ (34) = 2.41$, $p < .02$, as depicted in Table 8. Individuals with early onset left lesions were found to have a significantly shorter right foot (mean = 0.26) whereas individuals with early onset right lesions had a smaller left foot (mean = 0.18).

All left handed subjects (n = 33) were then classified into one of four groups as suspect for pathological

Table 8

Pedal Asymmetry Means by EEG Focus
(Focal Lesions Only)

Group	EEG Focus	Total	Mean Asymmetry (cm)	t Value	df	Significance Level
1	R	18	0.18	2.41	34	$p < .02$
	L	18	-0.26			
2	R	27	0.05	1.37	36.8[a]	NS
	L	24	-0.15			
3	R	22	0.45	-1.10	60	NS
	L	40	0.16			
ALL	R	67	0.08	1.21	146	NS
	L	82	-0.04			

[a]Variances unequal. A t test for unequal variances is reported.

left-handedness. An analysis of variance of pedal asymmetry across these four "suspect groups was significant, $F(3,28) = 5.17$, $p < .0005$.[8]

Post hoc analyses of mean differences revealed that the significant asymmetry differences occur between the high suspect (mean = - 082) and not suspect (mean = 0.16) groups at the 0.5 significance level (Table 9). A Spearman rank order correlation revealed a significant relationship between pedal asymmetry and the different suspect groups, $r_s = -0\ 67$, $p <\ 0001$, with 44% of the variability in asymmetry accounted for by the different suspect ranks The subjects were then dichotomized into PLH+ (suspect Groups 3 and 2) or PLH (suspect Groups 1 and 0). Pedal asymmetry was significantly different for these two groups, $F(1,30) = 15.39$, $p <\ 005$ PLH classification (+ or) accounted for 34% of the variability in pedal asymmetry, the mean pedal asymmetry was 14 cm and -.69 cm for the PLH- and PLH+ groups respectively.

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[8]One sinistral with an early onset left lesion has a history of spastic diplegia, and was omitted from this analysis because she is an atypical subject from a different and identifiable population. This individual is reported to have two distinct lesions, one located in her left temporal lobe, and a second at the pontine-cerebellar junction, at the point of efferent fiber decussation. Consequently, this individual has a right upper extremity monoplegia and a left lower extremity paraplegia. Thus, while the former lesion is that of interest in this investigation, likely causing her manifest left hand preference, the latter lesion has caused a differential involvement of the lower limbs.

Table 9

Duncan's Multiple Range Test for Mean Differences Between Suspect Groups

Suspect Group	Total (n)	Mean Asymmetry[a]
(0) Not suspect	19	0.16
(1) Low	2	0.00
(2) Moderate	5	-0.54
(3) High	6	-0.82

[a]Mean of Group 3 significantly different from Group 0, $\underline{W}_3$ (28), at $\underline{p} < .05$.

Given that a comparison of pedal asymmetry does differentiate those sinistrals at risk for PLH from those not at risk for PLH, the above sample means and variances were substituted into the classification function formula described on page 37 and a cutoff point pedal asymmetry was determined. It was found that if a left hander has a pedal asymmetry > - .5 cm (smaller right foot) he or she is a high suspect for PLH.

Using this cutoff point, four of seven sinistrals from the high suspect group were identified. Although the subject with spastic diplegia did not meet the pedal asymmetry cutoff point secondary to the contralateral lower limb involvement, her early onset left focal lesion and right upper extremity spasticity would also make her suspect for PLH. If these five sinistrals are pathological left handers the incidence of PLH in the early onset left focal lesions group would be 71.4%.

A closer investigation of those subjects from the moderate suspect group revealed that four of these five sinistrals report that they were initially right-handed, but have switched to a left-hand preference secondary to trauma, surgery or illness.[9] By definition, these manifest

[9]One subject became left handed secondary to a left anterior head trauma at age 7 (ID# 127), one became left handed secondary to a left frontal lobectomy at age 7 (ID# 125), one became left handed following a vascular accident secondary to sickle cell anemia at age 14 (ID# 102).

left handers would be presumed pathological left handers The overall incidence of predicted and presumed PLH in all sinistrals with left focal lesions is found to be 64.5%.[10]

However, while these four individuals are, by definition, pathological left-handers, only one of these individuals, with a 2.7 cm asymmetry secondary to a left frontal lobectomy at age 7, falls beyond the cutoff point asymmetry score If this subject is deleted from the moderate suspect group, the mean asymmetry in this group becomes zero, which is equivalent to that seen in the low suspect group (Tables 9 and 10) Neither of the two low suspect group sinistrals fell beyond the cutoff point One of the 19 non-suspect sinistrals fell beyond the .5 cm criterion, but this is not significantly different from chance occurrence Table 10 further illustrates that there was no sex, CT or familial sinistrality effect for the predicted or presumed pathological left-handers.

Table 11 reveals that the frequency of familial sinistrality is not significantly lower in dextrals and high suspect pathological left handers, who would be presumed to be natural dextrals.

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and one switched to a left hand preference following a left temporal lobectomy at age 14 (ID# 124).

[10] If as the results of Tables 7 and 8 suggest, there is no relationship between handedness of pedal asymmetry and focal EEGs in individuals with late onset seizures, the two sinistrals with late onset left lesions who report that they have always been left-handed might then be considered as not suspect for PLH. In this case the overall frequency of predicted or presumed PLH would be 75%.

Table 10

PLH Suspects

Suspect Group	ID #	Onset	Sex	Asymmetry	EEG	FS	CT
	95	Birth	M	-0.4	LF	-	NL
	98	Birth	M	-0.6	LT	+	*
High Suspect	157	Birth	M	-1.5	LF	-	NL
(3)	129	Birth	F	-1.1	LF	+	L
	130	1	F	-1.0	LT	+	NL
	131	Birth	F	-1.0	LT	-	*
	128	2	F	-0.3	LT	-	L
High Suspect	96	5	M	0.3	LP	-	NL
(2)	102	14	M	0.0	LP	+	*
	124	14	F	-0.1	LT	+	*
	125	7	F	-2.7	LP	-	*
	127	7	F	-0.2	LA	-	L
Low Suspect	97	48	1	-0.1	LA	+	L
(1)	99	22	1	0.1	LT	-	NL

FS = Familial Sinistrality
LA = Left Anterior (nonspecific)
LF = Left Frontal
LT = Left Temporal
LP = Left Posterior
L = Left Hemisphere involvement
NL = Normal
* = No CT

Table 11

Frequency of Familial Sinistrality for High Suspect Sinistrals, Non Suspect Sinistrals and Dextrals

Familial Sinistrality	High Suspect	Non Suspect	Dextrals	Total (%)
-	4	10	141	155
(%)	(57.1%)	(55.6%)	(58.7%)	(58.5%)
+	3	8	99	110
(%)	(42.9%)	(44.4%)	(41.3%)	(41.5%)
TOTAL	7	18	240	265

χ^2 NS

DISCUSSION

The results of this study confirm the hypothesized relationship between early focal brain trauma, manifest hand preference and pedal asymmetry, suggesting that the presence of a markedly smaller (by > .5 cm) right foot in a left handers with a left focal lesion may signal the presence of PLH. Before exploring the nature of this relationship, the group and handedness classification used in the interpretation of these data will be addressed.

Handedness

Studies addressing the relationship between handedness and hemisphere specialization have been hampered by the variety of methods used to assess handedness and by the likelihood that handedness is a continuous rather than dichotomous variable (Annett, 1967, 1972; Bingley, 1958, Brain, 1945). It has been emphasized that "handedness" reflects not only preferred writing hand, but hand preference and hand dominance on a variety of strength, rhythm, speed and skill tasks (Johnstone, Galin & Herron, 1979, Loo & Schneider, 1979; Preilowski, 1978). This may explain why self-classification of handedness and expressed writing hand

have been found to be unreliable estimates of manual or cortical dominance reflected on task performance particularly in sinistrals (Johnstone, Galin & Herron, 1979, Satz, Achenbach & Fennell, 1967). The Briggs and Nebes version of Annett's handedness inventory has been found to be a useful readily scorable assessment of manual preference, tapping three aspects of handedness power (strength), skill (dexterity, accuracy) and rhythm (motion, movement such as sweeping, etc.). It has also been found to be reliable and internally consistent (Loo & Schneider, 1979) A self report inventory is preferable to other tests of manual preference because of each of administration and since it has been found to be " . . . a more comprehensive measure of handedness than any single performance measure" (Johnstone et al., 1979, p. 79).

Although handedness is not a dichotomous measure, interpretation and presentation of the data are difficult if one cannot make comparisons between dextrals and sinistrals With the knowledge that some information may be lost when dichotomizing this measure, handedness was classified according to a cutoff score which maximized the correct classification of stated hand preference This procedure is felt to be preferable to the arbitrary cutoff used in the Johnstone et al. (1979) study.

The cutoff point, falling between 36 and 37, is intuitively logical, as a midpoint score (36 on a 12-60 scale) would suggest that an individual is truly ambidexterous, having endorsed on equal number of left and right hand preference items. A score above 36 would suggest a right hand preference, while a score below 36 indicates a left hand preference. Closer investigation of the data revealed that the one self-classified dextral who was differentially classified following the implementation of this cutoff criteria scored just below the cutoff (35) while the two self-classified sinistrals scored well into the "right handed" range (44 and 47). This is consistent with the Satz et al. (1967) finding that some self-classified sinistrals demonstrate a strong right-sided preference.

Group (Onset Age)

Comparison of seizure and control subjects necessitated the formulation of discrete groups because the control subjects, with the exception of a few trauma victims, did not have an identifiable onset age.

Within the experimental sample, when the etiology of the seizure was known (e.g. trauma, infection, neoplasm), the age at that point, rather than seizure onset age was used to determine group classification. This follows evidence that,

particularly in cases of perinatal injury, epilepsy may not develop until years after the acute episode, as alterations in the "convulsive threshold" change with age (Laidlaw & Richens, 1976, p. 73). Similarly, post traumatic epilepsy in later years may not develop until months or, on occasion, years later (Paillas, Paillas & Bureau, 1970). When the etiology of the seizures was unclear or unknown, the subject's age at the time of seizure onset was used for group classification.

In accordance with the model of PLH proposed by Satz, early onset was defined as seizure onset from birth to age 2. Late onset was defined as that occurring after the age of 17. Seventeen was selected to minimize the likelihood that maturational differences could account for any observed pedal asymmetries.[11] Middle onset classified those remaining individuals whose etiology or seizure onset occurred from age 2 through adolescence (age 17). With the deletion

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[11] The Levy and Levy (1978) study reported that the most robust pedal asymmetries were observed in children. To minimize the maturational effect on observed pedal asymmetries, the Yanowitz et al. (1981) replication study, and for consistency the present investigation, required a minimum age of 17 for participation. In addition, with the inclusion of VA subjects, a classification age of 17 makes empirical sense, such that all VA subjects with post-traumatic epilepsy would fall into the late onset group.

of the VA subjects, whose inclusion would spuriously inflate the frequency of late onset seizures, it was found the 30% of seizures developed by age 2, 49% through adolescence, and 21% in adulthood (Table 4). This is consistent with the incidence reported by the Epilepsy Foundation of America (1980). They report that 30% of all epilepsies manifest in the preschool years, 48% during school years, with 23% developing in adulthood.

Handedness, EEG and Pedal Asymmetry

Figure 1 reveals an intriguing finding. In the experimental groups (1-3), the relationship between handedness and pedal asymmetry was significant only in the early onset group (Group 1), with left-handers having smaller right feet, and right-handers having smaller left feet. While this is consistent with the hypothesis that an early lesion may produce an alteration in pedal development, a surprising finding was observed in the control group, where the opposite relationship was seen. While this appears to add a new finding to the myriad of studies debating the relationship between cortical and somatic asymmetries it may more likely represent sampling error resultant from the small number of sinistrals (six) in the control group. The results from this investigator's previous work (Yanowitz, Satz & Heilman,

(1981) found no difference in the direction of pedal asymmetries for dextrals and sinistrals when a larger sample of normal sinistrals was used (n = 53).

Secondly, it is incorrect to suggest that there is a foot size difference in dextrals. No group differences existed (Figure 1). Although the foot differences in the Group 0 and 1 dextrals differ significantly from the sinistrals, they are not significantly different from each other.

It is also possible that the pedal asymmetry observed in the control subjects reflects a true difference secondary to some effect that was not measured in this study. Although Levy and Levy (1978) argue that this asymmetry may reflect differential effects of fetal sex hormones, no sex effect was observed. Moreover, Pomerantz and Harris (1980) attempted to replicate the Levy and Levy findings using a sample of 7- 11- and 15-year old dextrals. Not only were they unsuccessful, but when a significant asymmetry was observed, it favored a shorter left foot in both males and females.[12] They concluded that "Fetal hormonal

[12] The results published were found to be inconsistent, with the results printed in the article abstract disagreeing with that reported in the body of the text. Personal communication with the second author revealed that both the 15-year-old males and 11-year-old females had shorter feet.

factors . may -or may not--influence the development of other body regions. The questions are separate and separable' (p 678). Finally, the previous studies do not report the criteria used to assess handedness As we have seen, if verbal report is used, this may produce an inaccurate assessment It is possible that the discrepant results are related to the differential methods of assessing both handedness and of measuring pedal asymmetry (see Pomerantz & Harris, 1980, for review) A direct comparison of results may be impossible until a consistent measurement technique is used.

Although the relationship between handedness and asymmetry, particularly in control subjects, is inconclusive, a relationship between onset and location of lesion, handedness and pedal asymmetry is evident (Tables 7 and 8). Following the Satz model of PLH, which assumes the presence of a unilateral lesion, subjects with generalized or bilateral lesions were excluded from further investigation This is consistent with studies of cortical and hand dominance in hemidecordicates (e.g. Dennis & Whitaker, 1977) and seizure surgery patients (Bingley, 1958, Branch et al , 1964, Penfield & Roberts, 1959, Rasmussen & Milner, 1977) who by definition would have focal lesions. When all subjects with focal lesions are combined, no relationship

between EEG focus, handedness and pedal asymmetry is seen (Tables 7 and 8). However, a closer investigation reveals that the inclusion of late onset seizure patients obscures the underlying relationship seen in individuals with early onset seizures. A significant relationship between EEG focus and pedal asymmetry is observed in subjects with early onset focal seizures (Group 1). Subjects with left focal lesions are found to have smaller right feet, while the opposite is seen in subjects with right focal lesions (Table 8). This suggests that a lesion to one hemisphere results in hypodevelopment of the contralateral lower limb. The subjects in Group 2 reveal a similar trend, but the pedal differences are not significant. This suggests that lesions occurring after age 2 may produce some alteration in limb development, but this difference is not statistically significant. The subjects in Group 3 show a slightly larger right foot regardless of lesion focus, which would be consistent with the findings of Pomerantz and Harris. However, again these differences are not significant. It then seems that late onset lesions do not produce an alteration in the developed foot.

The incidence of left focal lesions in left- and right-handers is remarkably consistent with the mathematical

predictions posed by the (1972, 1973) Satz model in Groups 1 and 2 (Table 7) reflecting a strong relationship between early onset left focal lesions and manifest left-handedness.[13] Moreover, while the frequency of left handedness is not significantly different across groups when subjects with non-focal lesions are included (Table 4), the incidence of left-handedness in subjects with early onset focal seizures is 22.2% (Table 7), which is consistent with that reported in the studies employing subjects with perinatal or early brain traumas such as retardates and early onset seizure subjects (e.g. Brain, 1945, Gordon, 1920, Silva & Satz, 1979). Like Penfield and Roberts (1959), when these sinistrals with onset before age 2 are separated, the frequency of left-handedness parallels that observed in the control subjects (12%) (see Tables 4 and 7).

A closer investigation of the 33 sinistrals revealed several fascinating findings. First, all eight sinistrals with early onset seizures had focal lesions.[14] Laidlaw and

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[13]When adjusted for asymmetries in EEG data (favoring the left) the model predicts the incidence of left lesions in sinistrals to be 0.84 (Silva & Satz, 1979).

[14]Only 60% of right-handers from Group 1 had focal lesions.

Richens (1976) report that "generalized provocations such as (birth) asphyxia . . . may cause focal seizures in infancy and childhood . . . Fits following hemiplegic cerebral palsy (and) birth injury . . . are commonly focal" (p. 78). This would support Bakan's (1978) suggestion that the left hemisphere is more susceptible to the focal effects of birth hypoxia, and the increased frequency of manifest left-handedness in individuals with early left focal lesions may well represent PLH.

Secondly, with the exception of the individual with spastic diplegia these early onset sinistrals with left focal lesions who would be high risk suspects for PLH all had a smaller right foot, with four of the seven falling beyond the cutting point criterion for suspicion of PLH. Even more fascinating is the observation that of the five sinistrals in Group 2, four of whom state that their hand preference had changed following trauma, illness, or surgery, only the one individual who underwent a radical surgical procedure demonstrated this pedal asymmetry. This would suggest that beyond age 2, focal lesions can continue to produce an alteration in manifest hand preference, but a corresponding alteration in pedal asymmetry in not seen. Several explanations can be entertained. One could speculate that the greater quantity of sensory and motor cortex

devoted to the hand relative to the foot (Penfield & Jasper, 1954) would increase the likelihood that a discrete lesion would affect hand development more so than foot growth. However, sensory and motor cortex, which would be involved in the manifestation of hand or foot preference, is not necessarily responsible for the bone development of these limbs. Dreifuss (1956) reported that bone changes secondary to early onset hemiplegia seemed to be related to limb disuse resulting from motor weakness. Possible sensory loss effects were considered to augment these motor weaknesses. However, the exact relationship between brain and limb development remains uncertain. Alterations in blood supply to the limbs have been reported to produce trophic limb changes, with the elimination of vasoconstrictor function promoting bone growth by increasing blood supply (Grinker et al., 1959, p. 359). Thus, there appears to be subcortical involvement in bone development, specifically sympathetic autonomic nervous system involvement, as this is known to regulate blood flow (Gardner, 1968). Lesions in the temporal lobe could affect underlying hypothalamic structures, which could in turn disrupt the regulation of blood flow. This is supported by the observation that temporal lobe epileptics often manifest evidence of autonomic involvement

(tachycardia, sweating, pupillary dilitation, drop in blood pressure) (Laidlaw & Richens, 1976).

A second explanation for the presumed relationship between cortical trauma and pedal asymmetry arises from studies addressing the relationship between cortical speech representation changes and manifest left handedness. Rasmussen and Milner (1977) found that "an early lesion that does not modify hand preference is on the whole unlikely to change the side of speech representation" (p.359). Moreover, injuries to the left hemisphere after age 5 rarely changed the pattern of speech representation, but rather intrahemispheric reorganization occurred as the compensatory mechanism (p. 367). These findings could account for the observed changes in pedal asymmetry in the early onset left lesion sinistrals if a change in cortical speech representation also corresponds to changes in pedal development. In general, it appears that handedness may be altered without shifts in cortical speech representation or pedal development. However, when changes in cortical speech representation or pedal development occur in conjunction with the manifestation of left handedness in cases of early left focal lesions it seems plausible to infer that the manifest left handedness is secondary to the injury (PLH).

Finally, the frequency of presumed or predicted PLH in sinistrals with left focal lesions was found to closely parallel the incidence predicted by the Satz model (71%) when late onset seizure patients were excluded. This finding, in conjunction with the reduced incidence of left focal lesions in sinistrals with late onset seizures relative to that observed in left-handers with seizures developing through adolescence, suggests that the Satz model may require some modification to account for the differential effects of onset age on the freq[illegible]ency of left focal lesions and PLH in left-handers.

Sex, Familial Sinistrality and CT Scan Results

While the hypothesized relationship between early onset left focal lesions, manifest left handedness and lateralized pedal asymmetry (R < L) was supported in the present findings, the expected sex and family history of sinistrality effects were not. No sex effects were found when analyses were performed on all 280 subjects, on those 146 subjects with focal lesions or on the 33 sinistrals. Similarly, Table 11 reveals that left handers had no gre[illegible] incidence of familial sinistrality than either left-[illegible] suspect for PLH (presumed natural dextrals) or dextr[illegible] This could be a result of the less stringent criter[illegible]

to determine a positive history of familial sinistrality, which would more correctly be described as "non dextrality". Any individual who reported that any of his full siblings or natural parents were either left-handed or ambidexterous was classified as having a positive history of familial sinistrality. However, Kocel (1977) reported that "strong left-handers were no more likely to have familial sinistrality (53.9) than strong right-handers (45.7%)" (p. 237). Similarly, Bingley (1958) noted that the probability of finding someone with a left handed relative is high in a right hander (23%) and even higher in a left hander (48%), adding that in any individual case, knowledge of familial handedness gives very little information regarding the individual's natural handedness (p. 43).

Finally, CT scan results did not differentiate natural from pathological left-handers. Table 6 reveals that when CT scans were abnormal, they correlated highly with EEG findings. However, CT scans were abnormal in only 27.5% of the subjects with focal lesions, a result consistent with one reported by Bauer, Mayr and Pallua (1980), who found that 29% of individuals with chronic partial epilepsy of focal origin had focal CT scan abnormalities. Reisner, Zeiler and Wessely (1978) report that in subjects with post traumatic epilepsy, CT scans were found to be normal in 22%

of the cases, and localized lesions were seen in only 70.3% of the cases. While EEGs are useful in making functional diagnoses of epilepsy, reflecting electrical disturbances at the cellular level, CT scans will reflect only morphological alterations of cerebral tissue (e.g. density changes secondary to cell necrosis or proliferation, as in cases of neoplasm). Electrical disturbances arising from otherwise living tissue will be unlikely to produce positive CT scan findings.

Implications for Further Research

The relationship between early left focal lesions and lateralized pedal asymmetries in sinistrals provides support for the development of pedal asymmetry measures as a useful clinical tool to differentiate normal from pathological left-handers in the absence of clinical data. When a pedal asymmetry is seen, with the right foot being smaller by at least .5 cm, it provides compelling evidence that the sinistral may be a PLH, since this asymmetry is only seen in those left handers who incurred an early left lesion. The diagnostic utility of this tool is clear. While pedal asymmetries appear to have predictive utility for PLH suspect group membership, one must take caution when moving from group comparisons to individual prediction. Moreover,

further documentation of the relationship between alterations in foot growth and corresponding alterations in cortical dominance would be required before this technique could be considered to be a valid measure of altered brain development. Assessment of cortical speech representation in sinistrals suspect for PLH who demonstrate this lateralized pedal asymmetry would be useful.

Secondly, this study is limited by the absence of individuals with seizure onset between the ages of 2 and 5. Rasmussen and Milner (1977) suggest that changes in speech representation can occur through age 5. Any investigation exploring the relationship between sinistrality, pedal asymmetry and cortical dominance must include subjects with seizure onsets in this range to determine better the critical onset age affecting alterations in cortical dominance and corresponding functional or somatic asymmetries.

SUMMARY AND CONCLUSIONS

The relationship between handedness, brain trauma (EEG focus and onset), CT scan findings, sex, history of familial sinistrality and pedal asymmetry were addressed in 230 epileptic adults and 50 control subjects to explore the possibility of using pedal asymmetries to assist in the differentiation of normal from pathological left handers. A significant group by handedness interaction was found, revealing that in early onset seizure patients (Group 1) left-handers had smaller right feet, while right handers had smaller left feet. The reverse was found in control subjects.

The incidence of left-handedness was not significantly different across groups when all subjects were compared. Inclusion of only subjects with focal lesions, in accordance with the Satz (1972, 1973) model of PLH revealed a significantly greater frequency of manifest left-handedness in Group 1. Similarly, the observed frequencies of left focal lesions in sinistrals and dextrals paralleled that predicted by the Satz model only for individuals manifesting seizures before adulthood. Similarly, with the exclusion of the late onset seizure group, the incidence of predicted or

presumed PLH was also consistent with the mathematical predictions from the Satz model The model fails to account for the differential effect of late onset seizures, and may require revision.

A comparison of sinistrals highly suspect for PLH secondary to lesion location (left) and onset (before age 2) with sinistrals not suspect for PLH (seizure patients with lesions other than of left focal origin or control sinistrals) revealed that the former subjects had a lateralized pedal asymmetry, with a significantly smaller right foot A pedal asymmetry of > 5 cm (right foot smaller) predicts classification into the high suspect for PLH group. With the exception of one individual with gross cortical surgical defects, sinistrals who became left-handed following illness, trauma or surgery after the age of 2 did not show this pedal asymmetry. This resilience to change relative to the handedness change is consistent with that reported for cortical speech representation. The relationship between pedal asymmetry and cortical speech dominance is in need of further investigation A further evaluation of those sinistrals from Group 1 (early onset left focal lesions) would be warranted.

Sex, family history of sinistrality and CT scan results did not differentiate those left-handers suspect for PLH from those not suspect for PLH.

APPENDIX A

INFORMED CONSENT FORM

The purpose of this study is to explore the relationship between the development of the brain, hand dominance, and differences in body development - specifically the differences in foot size.

I understand that I will be one of approximately 300 subjects participating in this study, all of whom have had EEG's taken.

For my part in this study, I will be asked to complete a questionnaire about my hand preference and that of my family members. I will further be asked to remove my shoes and socks, to stand on a large sheet of paper, so that the researchers may trace my feet.

It has been found that tracing feet may tickle a bit. Other than that, there are no anticipated risks or discomforts to me. I further realize that there are no direct benefits to me. However, investigators hope that this study can help the physicians to learn more about brain function

The investigators will be happy to answer questions that I may have about this study I am also aware that all information obtained from me, my doctor or my chart will be strictly confidential No identifying information will be used in any publications stemming from this investigation. I am free to withdraw my involvement in this study at any time.

In the event of my sustaining a physical injury which is proximately caused by this experiment, professional medical care received at the J. Hillis Miller Health Center exclusive of hospital expenses will be provided me without charge. This exclusion of hospital expenses does not apply to patients at the Veterans Administration Medical Center who sustain physical injury during participation in VAMC approved experimental studies.

I have read and understand the above described procedure in which I am to participate and have received a copy of this description.

SIGNED ______________________________

DATE ______________________________

APPENDIX B

CLASSIFICATION OF ABNORMAL EEG LOCALIZATION

1. Maximal involvement left frontal lobe
2. Maximal involvement left temporal lobe
3. Maximal involvement right frontal lobe
4. Maximal involvement right temporal lobe
5. Multifocal or unspecified left anterior lobe abnormality
6. Multifocal or unspecified right anterior lobe abnormality
7. Maximal involvement left parietal lobe
8. Maximal involvement left occipital lobe
9. Maximal involvement right parietal lobe
10. Maximal involvement right occipital lobe
11. Multifocal or unspecified left posterior lobe abnormality
12. Multifocal or unspecified right posterior lobe
13. Bifrontal involvement
14. Bitemporal involvement
15. Unspecified bi-anterior involvement
16. Biparietal involvement
17. Bi-occipital involvement
18. Unspecified biposterior involvement
19. Generalized abnormality

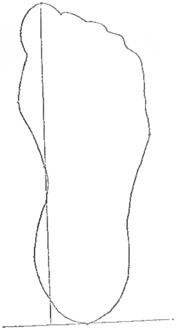
APPENDIX C

CLASSIFICATION OF ABNORMAL CT SCAN REPORTS

1. Focal atrophy - left
2. Focal atrophy - right
3. Diffuse atrophy
4. Increased density - left
5. Increased density - right
6. Increased density - diffuse
7. Decreased density - left
8. Decreased density - right
9. Decreased density - diffuse
10. Ventricular dilitation - left lateral ventricle
11. Ventricular dilitation - right lateral ventricle
12. Ventricular dilitation - 3rd or 4th ventricle
13. Ventricular dilitation - left and right ventricles
14. Atrophy and ventricular dilitation - left
15. Atrophy and ventricular dilitation - right
16. Density change and ventricular dilitation - left
17. Density change and ventricular dilitation - right
18. Density change and ventricular dilitation - diffuse

APPENDIX D

SCHEMATIC DIAGRAM OF METHOD OF FOOT MEASUREMENT



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BIOGRAPHICAL SKETCH

Joanne Sue Yanowitz was born on June 26, 1953, in New York City, and grew up in New Rochelle, New York. She was graduated from Vassar College in 1975, with Departmental Honors in Biopsychology.

Leaving her snow skis behind, she moved to Gainesville, Florida, to pursue her doctoral degree in clinical psychology. She enjoys bridge, good wine and a good joke. The story of her life can best be summed up by the following anecdotal story:

A novice high school teacher watched, with mixed emotions, her class taking their first true-false examination. She spotted a young man in the back of the room flipping a coin as he recorded his responses. "What are you doing?" the teacher queried. "I'm taking the test. Heads is true and tails is false."

While this distressed the teacher a bit, she permitted the student to continue with his test strategy. Shortly before the end of the examination, she spotted the student furiously flipping his coin and staring at his answer sheet.

"What are you doing now? It's time to turn in your paper," the teacher stated emphatically.

"I know," replied the student. "I'm just checking my answers."

Joanne hopes to modify her strategy when she assumes her clinical responsibilities in Atlanta, Georgia.

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Warren J. Rice

Warren J. Rice, Chairman
Associate Professor of
Clinical Psychology

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Hugh Davis

Hugh C. Davis, Jr.
Professor of Clinical
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Associate Professor of
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June 1981

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